

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

761081Orig1s000

Trade Name: Trazimera, 420 mg/vial for injection, multi-dose vial

Generic or Proper Name: Trastuzumab-qyyp

Sponsor: Pfizer Ireland Pharmaceuticals

Approval Date: March 11, 2019

Indication: TRAZIMERA is a HER2/neu receptor antagonist indicated for:

- The treatment of HER2-overexpressing breast cancer.
- The treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma. Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

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APPROVAL LETTER



BLA 761081

BLA APPROVAL

Pfizer Ireland Pharmaceuticals
Attention: Scott C. Anderson, MS
10646 Science Center Drive
San Diego, CA 92121

Dear Mr. Anderson:

Please refer to your Biologics License Application (BLA) dated June 22, 2017, received June 22, 2017, submitted under section 351(k) of the Public Health Service Act for Trazimera (trastuzumab-qyyp), 420 mg/vial for injection, multi-dose vial.

We acknowledge receipt of your resubmission dated September 28, 2018, which constituted a complete response to our April 20, 2018, action letter.

LICENSING

We have approved your BLA for Trazimera (trastuzumab-qyyp) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Trazimera under your existing Department of Health and Human Services U.S. License No. 2060.

Trazimera is indicated for:

Adjuvant Breast Cancer:

Adjuvant treatment of HER2-overexpressing node positive or node negative (ER/PR negative or with one high risk feature) breast cancer:

- as part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
- as part of a treatment regimen with docetaxel and carboplatin
- as a single agent following multi-modality anthracycline based therapy

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

Metastatic Breast Cancer:

- In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer
- As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

Metastatic Gastric Cancer:

- In combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma who have not received prior treatment for metastatic disease.

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture trastuzumab-qyyp drug substance at (b) (4)

The final formulated drug product and Bacteriostatic Water for Injection (BWFI), USP (containing 1.1% benzyl alcohol) will be manufactured, filled, labeled, and packaged at Pfizer Manufacturing Belgium NV, Puurs, Belgium (FEI: 1000654629). The final formulated drug product and BWFI will also undergo secondary packaging and labeling at (b) (4)

You may label your product with the proprietary name, Trazimera, and market it in 420 mg/vial for injection, multi-dose vial.

DATING PERIOD

The dating period for Trazimera shall be 48 months from the date of manufacture when stored at 2°C to 8°C. Vials may be stored at 30°C for a single period of up to 3 months, not to exceed the expiration date. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4) °C to (b) (4) °C in (b) (4) Drug substance (b) (4) the (b) (4) month expiry.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Trazimera and each kit component to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of Trazimera, or in the manufacturing facilities, will require the submission of information to your biologics license application for our review and written approval, consistent with 21 CFR 601.12.

APPROVAL AND LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information). Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (April 2018, Revision 5)*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved BLA 761081.**” Approval of this submission by FDA is not required before the labeling is used.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric studies requirement for this application because necessary studies are impossible or highly impracticable. Breast cancer and gastric cancer occur, for the most part in the adult population. The incidence of these cancer types in pediatric patients is extremely rare, and as such, clinical pediatric studies are impossible or highly impracticable.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

- 3565-1 Develop and implement a peptide mapping method for release and stability testing of trastuzumab-qyyp drug substance and drug product that can adequately assess levels of isomerized Asp102. Submit the final validation report and the release and stability acceptance criteria as a Prior Approval Supplement.

The timetable you submitted on February 22, 2019, states that you will conduct this study according to the following schedule:

Final Report Submission: 10/31/2019

- 3565-2 Re-evaluate trastuzumab-qyyp drug substance lot release and stability specifications for potency by the Fc γ RIIIa reporter gene assay and for the CEX-HPLC assay to quantify acidic, main, and basic species after 30 additional drug substance lots have been manufactured at the commercial scale. Submit the corresponding data, analysis, and statistical plans used to evaluate the specifications, and any proposed changes to the specifications as a Prior Approval Supplement.

The timetable you submitted on February 22, 2019, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/31/2021

- 3565-3 Re-evaluate trastuzumab-qyyp drug product lot release and stability specifications for potency by the Fc γ RIIIa reporter gene assay and for the CEX-HPLC assay to quantify acidic, main, and basic species after 30 additional drug product lots have been manufactured at the commercial scale. Submit the corresponding data, analysis, and statistical plans used to evaluate the specifications, and any proposed changes to the specifications as a Prior Approval Supplement.

The timetable you submitted on February 22, 2019, states that you will conduct this study according to the following schedule:

Final Report Submission: 03/31/2023

Submit chemistry, manufacturing, and controls protocols and all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled “**Postmarketing Commitment**”

Protocol,” “Postmarketing Commitment Final Report,” or “Postmarketing Commitment Correspondence.”

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the Prescribing Information, Medication Guide, and Patient Package Insert (as applicable) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>.

Information and Instructions for completing the form can be found at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For

more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements for licensed biological products (21 CFR 600.80).

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements for licensed biological products (21 CFR 600.81).

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
5901-B Ammendale Road
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
10903 New Hampshire Avenue, Bldg. 51, Room 4207
Silver Spring, MD 20903

If you have any questions, contact Clara Lee, Regulatory Project Manager, at (240) 402-4809.

Sincerely,

{See appended electronic signature page}

Laleh Amiri-Kordestani, MD
Supervisory Associate Director
Division of Oncology Products 1
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURES:

Content of Labeling
Prescribing Information
Carton and Container Labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

LALEH AMIRI KORDESTANI
03/11/2019 03:12:32 PM